Iron oxide catalyzed reduction of acid chlorides to aldehydes with hydrosilanes

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Iron Oxide Catalyzed Reduction of Acid Chlorides to Aldehydes with Hydrosilanes

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Abstract

Iron-catalyzed reduction of acid chlorides to the corresponding aldehydes with a hydrosilane as a reducing agent has been developed. A simple mixture of a commercially available iron oxide (FeO) and tris(2,4,6-trimethoxyphenyl)phosphine (TMPP) as a catalyst realized the reduction of acid chlorides to the corresponding aldehydes under mild reaction conditions.

Keywords:
Acid chlorides, Aldehydes, Hydrosilanes, Iron oxide, Reduction

1. Introduction

Acid chlorides are utilized as promising substrates in various organic reactions with transition-metal catalysts [1-5] because the oxidative addition of (acyl) carbon-chlorine bond to a low-valent metal center smoothly occurs [6]. Recently, we have reported iridium-catalyzed addition reaction of acid chlorides to terminal alkynes [7, 8]. Importantly, aliphatic acid chlorides as well as aroyl chlorides could be used in the addition reaction with suppression of decarbonylation and β-hydrogen elimination which have been two major intrinsic problems in transition-metal-catalyzed reactions [8]. We also found the palladium-catalyzed reactions of acid chlorides with hydrosilanes in the presence of allenes, giving α,β-unsaturated ketones regio- and stereoselectively [9].

The reduction of acid chlorides to aldehydes is one of important methods to afford aldehydes. The transformation with molecular hydrogen over supported heterogeneous palladium catalysts ($Pd/BaSO_4$) is well-known as the Rosenmund reduction [10]. However, in the reaction, the uptake of hydrogen must be monitored to avoid the over reduction. Homogeneous transition-metal catalyzed reductions of acid chlorides to the corresponding aldehydes have been also developed employing palladium [11] or ruthenium [12] as catalysts. Recently, we have reported a very efficient method of aldehydes synthesis from acid chlorides employing palladium catalysis and hydrosilane, which is stable, easy-to-handle and efficient reducing reagents [13]. Furthermore, we also developed the palladium-catalyzed reduction of carboxylic acids to the corresponding aldehydes in the presence of pivalic anhydride and hydrosilane [14]. Although these were good catalytic reactions, complexes of precious metals such as ruthenium and palladium must be used.

Recently, much attention has been paid to iron catalysts since iron is one of the most abundant metals on the earth. Efficient iron-catalyzed transformations including carbon-carbon bond forming reactions has been developed to date [15-19]. Regarding iron-catalyzed reductive transformations [20-31], iron complexes were found to be active for reductions of carbonyl compounds such as aldehydes [20, 21], ketones [20, 21], and amides [22]. However, some iron complexes must be prepared before use and they might be unstable for further handling [20, 21]. Therefore, iron-catalyzed transformation by the use of simple and commercially available catalyst precursors or in situ generated system is highly desired.

In the present study, we report that acid chlorides can be reduced to the corresponding aldehydes employing hydrosilane as a reducing agent in the presence of a catalytic amount of iron oxide (FeO) (99.9% purity). Iron oxides such as FeO or Fe_2O_3 are known as catalysts in dehydrogenation reaction [32], Fenton reaction [33], or Fisher-Tropsch reaction [34]. However,

to the best of our knowledge, there has been no precedent for the iron-catalyzed reduction of acid chlorides to aldehydes.

2. Experimental

2.1 General procedure

All manipulations were performed under an argon atmosphere using standard Schlenk-type glassware on a dual-manifold Schlenk line. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. THF and toluene were dried and purified before use by usual methods [35]. ^{1}H NMR spectra were measured with a JEOL ECX-400P spectrometer. The ^{1}H NMR chemical shifts are reported relative to tetramethylsilane (TMS, 0.00 ppm). The ^{13}C NMR chemical shifts are reported relative to $CDCl_3$ (77.0 ppm). GC analysis was carried out using Shimadzu GC-17A equipped with an integrator (C-R8A) with a capillary column (CBP-1, 0.25 mm i.d. × 25 m). Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectra were acquired on a SHIMADZU AXIMA-CFR Plus or a Bruker Autoflex using α-cyano-4-hydroxycinnamic acid as a matrix and NaTFA as a cationization reagent. Medium-pressure column chromatography was performed with a Biotage IsoleraOne. Column chromatography was carried out on silica gel (Kanto N60, spherical, neutral, 63-210 μm). TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F254. Iron oxide (FeO, 99.9% purity) was purchased from Aldrich and used without further purification.

2.2 Catalytic reaction

A typical procedure for the iron oxide catalyzed reduction of 3-phenylpropionyl chloride (**1a**) with H_3SiPh (Table 1, entry 1): iron oxide (3.6 mg, 0.050 mmol) and TMPP (6.7 mg, 0.013 mmol) were added to a 10 mL Schlenk flask with a magnetic stir bar. The flask was evacuated and backfilled with argon three times. Then, H_3SiPh (34 μL, 0.28 mmol) was added to the flask and the reaction mixture was stirred at 60 °C for 20 h under an argon atmosphere. Then, toluene (0.50 mL) was added to the flask and the resultant solution was stirred at room temperature for 5 min before **1a** (37 μL, 0.25 mmol) was loaded. Further, the reaction mixture was stirred at 60 °C for 20 h under an argon atmosphere. After cooling to room temperature, the reaction mixture was diluted with diethyl ether (5.0 mL) and tetradecane (50 μL, 0.19 mmol) as an internal standard was added. The yield of 3-phenylpropanal (**2a**; 57%) was analyzed by gas

chromatography. **2a** was isolated by silica gel column chromatography (hexane : EtOAc = 13 : 1). Pale yellow oil (16.8 mg) was obtained in 50% yield.

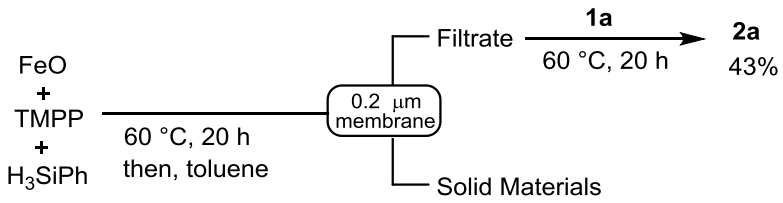
3. Results and Discussion

To study activity of an iron catalyst system, we carried out reduction of 3-phenylpropionyl chloride (**1a**) as a model reaction. When all these materials including FeO, ligand, hydrosilane and **1a** were mixed all at once, **2a** was obtained only in moderate yields with poor reproducibility. Thus, a mixture of FeO, tris(2,4,6-trimethoxyphenyl)phosphine (TMPP), and H_3SiPh was stirred at 60 ºC for 20 h. Then, toluene and **1a** were added, and the resulting mixture was further stirred at 60 ºC for 20 h. Under the reaction conditions, 3-phenylpropanal (**2a**) was obtained in 57% yield (entry 1). In the reaction mixture, 3-phenylpropionic acid was detected and its yield was determined as 32% by the GC internal standard method after derivatization to the corresponding methyl ester. This observation was in contrast to the palladium catalyzed reductions of acid chlorides [13], in which no carboxylic acids were formed. Without FeO, the conversion of **1a** was very low, and **2a** was obtained in only 4% yield (entry 2). Next, various iron precursors in place of FeO were employed. The reaction with Fe_2O_3 also afforded **2a** in 43% yield (entry 3), while other soluble iron precursors such as $FeCl_2$, FeF_2 and $Fe(acac)_2$ were not effective (entries 4–6). Without phosphine, the yield of **2a** considerably decreased (entry 7). Triphenylphosphine (PPh_3) was not efficient at all (entry 8). The reaction employing triarylphosphines with electron donating substituents afforded **2a** in moderate yields (entries 9-11). Other bulky phosphines such as tris(2,4,6-trimethylphenyl)phosphine and tricyclohexylphosphine afforded the product in low yields (entries 12 and 13). Thus, the addition of a catalytic amount of a phosphine affects the activity considerably. As for a hydrosilane, $HSiMePh_2$, $HSi(OEt)_3$, $H_2SiMePh$, H_2SiPh_2, and PMHS (polymethylhydrosiloxane) were less effective than H_3SiPh (entries 14–18 vs entry 1). As a solvent, the reaction in THF under otherwise the same reaction conditions as entry 1 afforded **2a** in 40% yield. Regarding catalyst loadings, we carried out the reactions in the presence of 10 mol%, 5 mol%, and 1 mol% of FeO (the ratio of FeO : TMPP was kept in 4 : 1), and in these reactions **2a** was afforded in 49%, 19%, and 21% yields, respectively. In addition, the ration between FeO and TMPP (4 : 1) was changed to 2 : 1, 1 : 1, and 1 : 2. As a result, the yield of **2a** was reduced to 50%, 40%, and 17% yields, respectively (Table S1, in the Supplementary data).

Various acid chlorides were reduced with H_3SiPh in the presence of FeO/TMPP catalyst system (Table 2). 3-Arylpropionyl chlorides with different substituents (4-Me, 4-OMe, 4-Cl,

4-CF_3, and 3-F) (**1b**–**f**) afforded the corresponding aldehydes (**2b**–**f**) in moderate yields (entries 1-5). Aliphatic acid chlorides such as **1g** and **1h** were also converted to the corresponding product (entries 6 and 7). Even sterically congested acyl chlorides such as **1i** and **1j** gave the products at higher reaction temperatures (entries 8 and 9). An acid chloride with an alkenyl moiety (**1k**) also afforded the corresponding aldehyde (**2k**) in 40% yield (entry 10). Although we examined the substrates with other functional groups such as ester, cyano, and nitro groups, the corresponding aldehydes were obtained only in trace yields. Unfortunately, aroyl chlorides (i.e., aromatic acid chlorides such as benzoyl chloride) could not be employed as substrates due to their low reactivities.

To gain some insight into catalytically active species, a reaction mixture of FeO, TMPP and H_3SiPh stirred at 60 °C for 20 h. After adding toluene, the mixture was filtered through a 0.2 μm membrane (13P, GL Science). Then, **1a** was added to a resulting pale yellow filtrate and the mixture was further stirred at 60 °C (Scheme 1). As a result, **2a** was obtained in 43% yield with 90% conversion of **1a.** Under the reaction conditions, carboxylic acid was detected as a side product. In addition, the separated dark brown *solid* was employed as the catalyst in the reaction of **1a**. In the reaction, a trace of **2a** was obtained with the low conversion of **1a** (18%). The result may suggest that some soluble iron species would be responsible for the present catalytic reaction. Unfortunately, various measurements including MALDI-TOF MASS and X-ray crystallographic analysis to characterize active species were failed.



Scheme 1. Filtration test.

4. Conclusion

In conclusion, we found that the ion-catalyzed reduction of acid chlorides employing hydrosilane as a reducing agent. A simple mixture of a commercially available and easy-to-handle iron oxide (FeO) and 2,4,6-trimethoxyphenylphosphine (TMPP) was found to be a good catalyst. Further application to reductive transformations and elucidation of the reaction mechanisms are now in progress.

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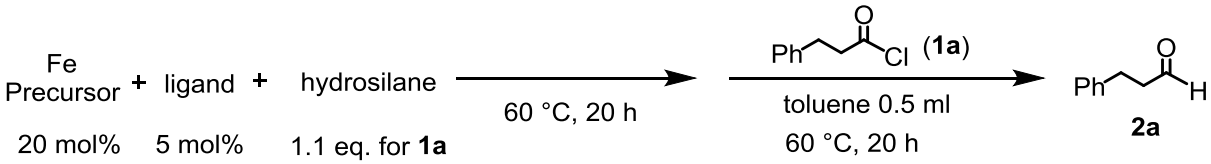
Table 1

Effect of iron precursors, ligands and hydrosilanes on the reduction of 3-phenylpropionyl chloride (**1a**).[a]



Entry	Precursor	Ligand	Hydrosilane	Conv. of **1a** (%)[b]	Yield of **2a** (%)[b]
1	FeO	TMPP	H_3SiPh	93	57 (50)[c]
2	none	TMPP	H_3SiPh	31	4
3	Fe_2O_3	TMPP	H_3SiPh	83	43
4	$FeCl_2$	TMPP	H_3SiPh	26	2
5	FeF_2	TMPP	H_3SiPh	33	5
6	$Fe(acac)_2$	TMPP	H_3SiPh	53	3
7	FeO	none	H_3SiPh	39	7
8	FeO	PPh_3	H_3SiPh	11	2
9	FeO	$P[2,6\text{-}(MeO)_2C_6H_3]_3$	H_3SiPh	32	15
10	FeO	$P(o\text{-}MeOC_6H_4)_3$	H_3SiPh	34	21
11	FeO	$P(p\text{-}MeOC_6H_4)_3$	H_3SiPh	91	28
12	FeO	$P(Mes)_3$	H_3SiPh	13	1
13	FeO	PCy_3	H_3SiPh	62	33
14	FeO	TMPP	$HSiMePh_2$	24	5
15	FeO	TMPP	$HSi(OEt)_3$	34	2
16	FeO	TMPP	$H_2SiMePh$	42	14
17	FeO	TMPP	H_2SiPh_2	46	13
18	FeO	TMPP	PMHS	89	4

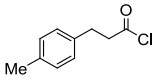
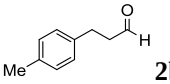
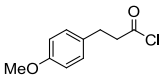
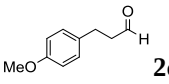
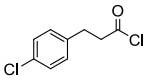
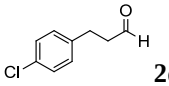
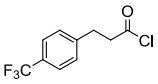
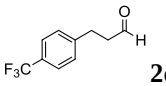
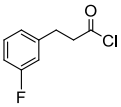
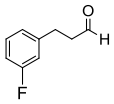
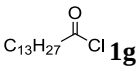
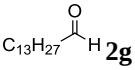
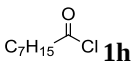
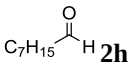
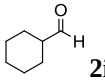
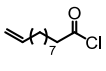
[a] Reaction conditions: iron precursor (0.050 mmol, 20 mol %), ligand (0.013 mmol, 5.0 mol %) and hydrosilane (0.28 mmol) at 60 °C for 20 h, then, **1a** (0.25 mmol) and toluene (0.50 mL) at 60 °C for 20 h .

[b] Determined by GC analysis based on the internal standard technique.

[c] Isolated yield of **2a**.

Table 2

Iron oxide catalyzed reduction of acid chlorides.[a]

Entry	Acid chlorides (**1**)	Teperature (°C)	Aldehydes (**2**)	Yield (%)[b]
1	 **1b**	60	 **2b**	45 (64)
2	 **1c**	60	 **2c**	44 (58)
3	 **1d**	60	 **2d**	44 (56)
4	 **1e**	60	 **2e**	58 (68)
5	 **1f**	60	 **2f**	53 (68)
6	 **1g**	60	 **2g**	36 (40)
7	 **1h**	80	 **2h**	(47)
8	 **1i**	100	 **2i**	(42)
9	 **1j**	120	 **2j**	(41)
10	 **1k**	60	 **2k**	40 (52)

[a] Reaction conditions: FeO (0.050 mmol, 20 mol %), TMPP (0.013 mmol, 5.0 mol %) and H_3SiPh (0.28 mmol) at 60 °C for 20 h, then, **1** (0.25 mmol) and toluene (0.50 mL) at 60~120 °C for 20 h .

[b] Isolated yield of **2**. Value in palenthesis showed GC yield based on the internal standard technique.